A Digital Pathology Solution for Immunohistochemistry

Digital IHC

User's Guide

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Part Number/Revision: MAN-0099, Revision B
Date: September 4, 2009

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User Resources

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Disclaimers

Use normal care in maintaining and using the Spectrum servers. Interrupting network connections or turning off the Spectrum and DSR servers while they are processing data (such as when they are analyzing digital slides or generating an audit report) can result in data loss.

This manual is not a substitute for the detailed operator training provided by Aperio Technologies, Inc., or for other advanced instruction. Aperio Technologies Field Representatives should be contacted immediately for assistance in the event of any instrument malfunction. Installation of hardware should only be performed by a certified Aperio Technologies Service Engineer.

ImageServer is intended for use with the SVS file format (the native format for digital slides created by scanning glass slides with the ScanScope scanner). Educators will use Aperio software to view and modify digital slides in Composite WebSlide (CWS) format.

Aperio products are FDA cleared for specific clinical applications, and are intended for research use for other applications. For clearance updates, visit www.aperio.com

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1 Overview

Aperio provides a complete Digital Pathology Solution for Immunohistochemistry (IHC)—Digital IHC™—that combines scanning, management, viewing and analysis of slides with reading IHC slides on a computer monitor, quantitative IHC image analysis* and professional reports, all integrated into an efficient clinical workflow.

This chapter provides an overview of Aperio's Digital IHC solution and its documentation.

The Immunohistochemistry (IHC) Workflow

A lab receives a specimen from a biopsy and prepares a block from which an H&E (Hematoxylin and Eosin) slide is prepared. The typical IHC (Immunohistochemistry) workflow starts with the diagnosis of cancer by a pathologist reviewing the H&E slide.

Once the pathologist has determined that a patient has cancer, he/she orders an IHC panel. An IHC panel consists of consecutively cut slides from the same specimen block that are then stained with different IHC stains. A typical IHC panel for breast cancer includes the following IHC stains: HER2 (Human Epidermal growth factor Receptor 2), ER (Estrogen Receptor) and PR (Progesterone Receptor). The pathologist then reads the IHC slides and provides a (semi-)quantitative assessment of the protein expressions. A report is generated for the oncologist. IHC quantification is used to determine the appropriate treatment options for the patient.

HER2 is a membrane stain. The pathologist assesses the intensity and completeness of the membrane staining of the tumor cells and determines a score of 0, 1+, 2+ or 3+ for the slide. HER2 is used specifically to assess Herceptin® (Trastuzumab) as a treatment option and to determine the aggressiveness of breast tumors.

ER and PR are nuclear stains from which the pathologist assesses the staining intensity of the nuclei of the tumor cells and determines the percentage of positive stained nuclei as a percentage between 0 to 100% and the average staining intensity of the positive nuclei as a score of 0, 1+, 2+ or 3+. Different labs use different scoring schemes for the nuclear stains. For example, some labs use only the percentage of positive nuclei as a score and use different cut-off thresholds of 1%, 5% or 10% for the interpretation; other labs use the percentage of positive nuclei and the average staining intensity of the positive nuclei to calculate a combined score like the Allred Score.

* Aperio's image analysis algorithms are FDA cleared for specific clinical applications, and are intended for research use for other application.

Here is an overview of the traditional clinical workflow. We highlight in blue where our Digital IHC Solution affects the traditional clinical workflow. Aperio's digital pathology system provides easy access to all case, specimen and slide information from the current and all previous biopsies, including the gross images, H&E slides, IHC slides, and controls. Our Digital IHC solution provides a new all-digital workflow for IHC, from glass slides to reports.

Who This Guide Is Intended For

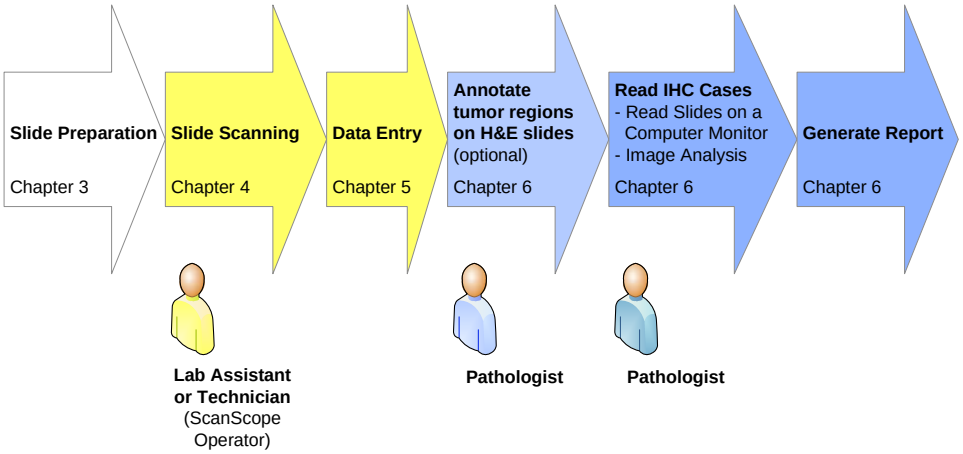
This guide is a reference document that covers all aspects of using Aperio's Digital IHC solution. Different steps of your IHC workflow may involve different people with different skills and responsibilities. Therefore, the chapters in this guide are organized by function so that a particular reader can go directly to the section of interest to him or her:

Functional Area	Responsible Person	Where to Find Information
Overview	All readers	Chapter 1, "Overview"
Compliance	Medical Director	Chapter 2, "Intended Use"
Ensuring that your glass slides are optimized for Digital IHC	Lab Manager	Chapter 3, "Slide Preparation"
Performing high quality slide scans and enter data	Lab Assistant or Technician (ScanScope Operator)	Chapter 4, "Scanning" Chapter 5, "Data Entry"
Step-by step instructions on how to read a case—everything the pathologist needs to know to use the system	Pathologists	Chapter 6, "Reading Cases Step-by-Step"

In addition, several additional documents are intended for personnel responsible for setting up and administering Digital IHC:

Functional Area	Responsible Person	Where to Find Information
Set up and configure Spectrum for your IHC workflow	Administrator	*Digital IHC Guide to Spectrum Setup*
Additional application description, set up instructions and performance specifications.	Administrator Pathologists Medical Director	*Digital IHC Application Guides* ■ *Breast/HER2 Digital Read* ■ *Breast/PR Digital Read* ■ *Breast/HER2/Dako Image Analysis* ■ *Breast/ER/Dako Image Analysis* ■ *Breast/PR/Dako Image Analysis* ■ *Membrane Image Analysis* ■ *Nuclear Image Analysis*

The illustration below shows a quick summary of the basic steps of the Aperio Digital IHC workflow and refers to the corresponding chapters in this document.



The Digital IHC Solution

Aperio's complete Digital IHC solution is based on several components:

- ScanScope glass slide scanner
- Spectrum Plus
- Barcode
- LIS Integration
- IHC Image Analysis
- Reporting

More Information

For more details on your ScanScope scanner, the Spectrum digital pathology information management system, the ImageScope slide viewer, and running Aperio image analysis algorithms, please see:

- The user's guide for your ScanScope instrument.
- *Spectrum/SpectrumPlus Operator's Guide.*
- *Spectrum/Spectrum Plus Administrator's Guide.*
- *Digital IHC Guide to Spectrum Setup*
- *ImageScope User's Guide.*
- *IQ Image Quality User's Guide*
- *Spectrum Plus Reporting User's Guide*

Meeting Regulatory Requirements

Spectrum Plus contains several features that assist your organization in complying with regulatory requirements such as FDA 21 CFR Part 11, HIPAA, and GLP. The optional Spectrum Compliance Module contains additional features that address specific regulatory requirements.

For more detailed information on the Compliance Module, please refer to the *Spectrum/Spectrum Plus Administrator's Guide*.

Patient Data Confidentiality

Spectrum provides a full security system that ensures that users can only access data they are authorized to see, thus protecting patient data from unauthorized access.

Digital slides and related meta-data reside in the Spectrum database. Spectrum uses the administrator/user structure that restricts security-sensitive actions to an authorized administrator. The administrator can:

- Set up users with passwords. Users must log into Spectrum with their username and password and be authenticated before they can access restricted data.
- Set up data groups that restrict access to specific data.
- Set users' access permissions to grant them full access, read-only access, or no access to the defined data groups.
- Assign users roles that limit the commands they can perform and data they can access.

2
Intended Use

Aperio's Digital IHC solution is intended to be used with different applications, some FDA cleared for In-Vitro Diagnostic (IVD) use and all others for Research Use Only (RUO).

In-Vitro Diagnostic Use

The following IHC applications are FDA cleared for In-Vitro Diagnostic (IVD) use. For specific information on those applications, refer to the application guides.

- Breast/HER2 Digital Read
- Breast/PR Digital Read
- Breast/HER2/Dako Image Analysis
- Breast/ER/Dako Image Analysis
- Breast/PR/Dako Image Analysis

Research Use Only

All other applications are for Research Use Only (RUO). Additional documentation is provided for the following applications.

- Membrane Image Analysis
- Nuclear Image Analysis

Caution: Federal (U.S.) law restricts this device to sale by or on the order of an appropriately licensed healthcare practitioner.

IMPORTANT

If the ScanScope is used in any manner not specified in this documentation, the protection provided by the equipment may be impaired.

WARNING: This equipment generates, uses and can radiate radio frequency energy. If not installed and used in accordance with the instructions in this manual it may cause interference to radio communications. It has been tested and found to comply with the limits for a Class A computing device (pursuant to Subpart B of Part 15 FCC Rules), which are designed to provide reasonable protection against such interference when operated in a commercial environment. Operation of this equipment in a residential area is likely to cause interference, in which case you, at your own expense, will be required to take whatever measures may be required to correct the interference.

3
Slide Preparation

Slide preparation has a considerable influence on how well slides can be scanned. Optimizing the slide preparation for scanning is a good idea to get the most out of your digital pathology system. Make sure to control the quality of your glass slides!

This chapter is for the lab manager who is responsible for the slide preparation.

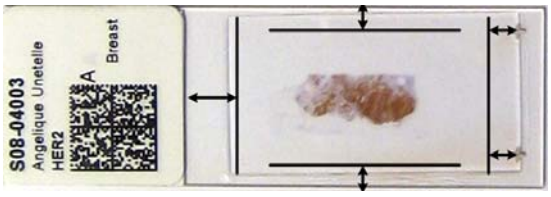
Tissue Preparation

The tissue preparation is important for scan quality. Folds in the tissue and tissue sections that are too thick will result in blurry images. Problems with blurry slides may require the preparation of a new slide.

Mechanics

The mechanics of the slide are important for its scan quality and ease of scanning. The slides should be in clean and good condition—no air pockets under cover slip, no dirt, no fingerprints, no markings, no writing, no extra adhesive, no broken slides, no chips, no scratches, no overhanging cover slip, etc.

The tissue ideally should be located in the middle of the slide a distance from the edges of the slide, the label and any other markings. It is helpful for the tissue to be placed consistently in the same location and orientation on the slide.



Make sure there is no glue around the edges of a slide that would cause it to stick or catch in the ScanScope stage area.

Keep the glue attaching the cover slip to a minimum. Excess glue makes it hard for the tissue finder to distinguish between actual tissue and the glue. If a focus point lands on the glue, slide focus will not be accurate.

Some of the mechanical problems of a slide can be resolved by cleaning the slide with a cotton rag (don't use chemical cleaners) or trimming the sides with a razor blade. Permanent problems with a slide may require the preparation of a new slide.

Staining

Reproducibility of the IHC stains is important for consistent and accurate scoring. Make sure that the variations of the staining process are controlled and eliminated to the greatest extent possible. Employ appropriate morphological studies and controls as specified in the reagent manufacturers' instructions.

Glass Slide Quality Control

It is the responsibility of the lab to verify the quality of the tissue preparation, the mechanics of a slide and the staining.

4
Scanning

For more detailed information on how to scan slides, please refer to the *ScanScope User's Guide*.

The imaging system and its calibration as well as the scanning parameters are critical to transforming a glass slide into a high quality digital slide. Aperio's ScanScope instruments allow slides to be scanned automatically. Make sure to control the quality of the digital slides!

This chapter is for the lab assistant or technician who scans the glass slides on the ScanScope.

Required Training

A ScanScope operator should be able to scan slides properly for the Digital IHC applications after self study of the *ScanScope User's Guide* for information on the general use of the ScanScope instrument and this chapter for specific information and requirements for the Digital IHC applications.

Imaging System

The most important property of any imaging system is its image quality. Aperio's ScanScope systems are based on Aperio's patented line-scanning technology which provides superior high-quality, high-resolution digital slides.

Calibration and Calibration Verification

Color and intensity reproducibility are important for the consistent and accurate scoring of IHC slides. The ScanScope systems provide a high degree of color and intensity reproducibility scan after scan and also from one ScanScope to another. Professional color management using ICC (International Color Consortium) profiles ensures that you always see the same "true" color calibrated image of a slide wherever and whenever you view it.

The ScanScope automatically calibrates each slide when it is scanned. The calibration at scan time is optimal, as it takes into account the characteristics of each slide and the system at the exact moment of the scan and not at the moment in time when a daily or factory calibration was performed.

The ScanScope automatically assures proper operation of the ScanScope for each scan by performing a test of each calibration that determines if there is a problem. In case of a problem, the scan is aborted. A calibration problem can have different causes, including problems with the light source, camera gains,

macro camera offsets, location of the slide on the tray, optical misalignment, etc. please see the troubleshooting section in the *ScanScope User's Guide* for more details.

The Spectrum administrator can print calibration reports for any range of dates.

> For information on printing calibration reports, see the *Spectrum/Spectrum Plus Administrator's Guide.*

Compression

Because of the large size of whole-slide images, Digital Pathology applications often use lossy data compression technologies such as JPEG and JPEG2000. Aperio's ScanScopes allow users to select JPEG or JPEG2000 image compression types and quality factors between 10 and 90.

The Digital IHC applications require that glass slides be scanned with **JPEG2000** compression (type 3 as defined in the ScanScope Console) with **quality factor 70**.

Sharpening

Aperio's ScanScopes provide the capability of applying a sharpening filter while the slides are scanned.

CAUTION: Using image filters may affect analysis of the image. While sharpening filters tend to provide a more pleasing image to the human eye, they may compromise analysis performed by analysis algorithms because the image has been altered.

The Digital IHC applications require that **no sharpening filter** is used.

Predefined Parameter Set for Scanning IHC Slides

It is important that all IHC slides are scanned with the required parameter settings.

Aperio provides the required parameter settings for IHC slides in the ScanScope Controller XML file, called the "IHC" parameter set.

The Digital IHC applications require that the "IHC" parameter set (or equivalent) be used for scanning IHC slides.

Resolution for IHC Slides

Pathologists using a standard microscope typically view IHC slides with a 20x objective which is required to view all relevant cell features for their IHC scoring. Aperio ScanScopes provide slide scanning at 20x and 40x.

Although scanning at 40x provides more detail, it also requires unnecessarily longer scan times and larger file sizes.

The Digital IHC applications require that IHC slides be scanned at **20x**.

Automatic "One-Touch" Scanning

Aperio's ScanScopes can scan slides automatically using "one-touch" operation.

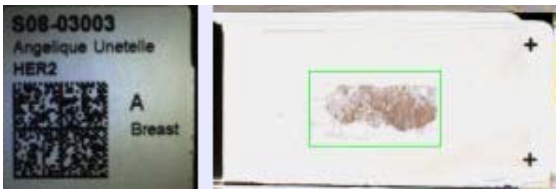
Digital Slide Quality Control

Ultimately it is up to the pathologist to look at digital slides to verify they are of sufficient quality to perform his/her task. In addition, ScanScope operators should verify digital slide quality after scanning.

The quality criteria that are important for the IHC image analysis system and that should be verified by the ScanScope operators are: (1) that the entire tissue sample has been scanned and (2) that the tissue is in focus.

Entire Tissue Sample Scanned

The ScanScopes provide a Macro Image, a low resolution image of the entire slide that also provides a green outline of the scanned area.



The Digital IHC applications require that the ScanScope operators look at the Macro Images of all the digital IHC slides and verify that the entire tissue sample was scanned.

Tissue in Focus

The ScanScopes provide a quality factor for each scan from 0 (worst) to 100 (best). Note that a low quality factor can be caused by poor slide preparation, like folds, thick tissue sections, air pockets under the cover slip, dirt, fingerprints, markings, writing, extra adhesive, broken slide, scratches, etc., but that the scan of the tissue still might be good—therefore the operator should not rely on the quality factor alone to determine the quality of a scan; he/she typically uses the quality factor as a triage tool to determine which slides he/she wants to review.

Rack	Slot	Quality Factor	Scan Status
0	1	98	Success

ScanScope operators should use the quality factor to triage slides for manual review and then review those slides by panning through the entire slide and verifying that the tissue sample is in focus.

The ScanScope operator should re-scan a slide if the entire tissue sample has not been scanned or if a tissue area is out of focus.

Manual Scanning

In some cases, the quality of a digital slide can be improved by manually scanning the slide. In other cases, it might be necessary to prepare a new slide. Manual scanning allows the ScanScope operator to designate the scan area, position the calibration area, place focus points, and focus the focus points manually.

The problem that the entire tissue sample has not been scanned can be resolved by designating the scan area manually and re-scanning.

To resolve the problem that a tissue area is out of focus, it helps to understand the cause of the problem; it might be a fold, thick tissue section, air pocket under the cover slip, dirt, fingerprint, marking, writing, extra adhesive, broken slide, scratch, etc. Some of the mechanical problems of a slide can be resolved by cleaning the slide with a cotton rag or trimming the sides with a razor blade. General guidelines to overcome focus problems are: place the focus points on the tissue and exclude the artifacts; place only a small number of focus points when the tissue is flat; place more focus points to adjust to a shaped tissue area; and use manual focus when the auto focus fails (for example in thick tissue).

5
Data Entry

For more detailed information on how to automate data entry or how to enter data manually, please refer to the *Spectrum/Spectrum Plus Operator's Guide*.

Data entry can be completely automated using barcodes and by integrating to your Laboratory Information System (LIS).

When a glass microscope slide is scanned by a ScanScope scanner, a licensed barcode on the slide label can be decoded to populate data fields in Spectrum Plus. Decoding barcodes requires some custom work, so contact Aperio Professional Services for assistance.

By integrating Spectrum with your Laboratory Information System, you can automatically transfer data between Spectrum and your LIS. Depending on how the integration is implemented, data from a slide's barcode that automatically goes into the Spectrum database can also automatically go into your LIS, or new or modified data in your LIS can automatically be copied into Spectrum. The integration requires custom work and your participation in deciding what information you want to share between the systems—contact Aperio Professional Services for assistance.

6
Reading Cases Step-by-Step

Aperio provides a complete solution for IHC that includes reading slides on a computer monitor, quantitative image analysis, and professional reports. This chapter provides step-by-step instructions on how a pathologist reads a case using Aperio's Digital IHC solution.

Aperio provides a new approach to IHC with an all-digital solution. Pathologists can now use quantitative image analysis conveniently with a click of a button while reading slides on a computer monitor.

Required Training

A pathologist should be able to use Aperio's Digital IHC solution and its applications after self study of this chapter and after referring to the information in the application guides.

Reading Digital Slides on a Computer Monitor

As with any change in diagnostic methodology, and especially one that relies on visual interpretation of complex images, a transition from conventional microscopy to digital microscopy presents the possibility of unintended but systematic change in diagnostic performance. Users should be aware that their IHC categorizations may be biased when switching from conventional to digital microscopy and as such, training beyond self study should be undertaken as needed to assure concordance before clinical adoption of the device. The laboratory is responsible for ensuring that concordance goals are reached and maintained.

Required Hardware and Software

A good monitor is a recommended investment for any pathologist who is viewing digital slides. Our *minimum* requirements for a computer monitor used for Digital IHC are the following:

Display Type:	Any high-quality LCD
Screen Resolution:	1680(h) x 1050(v) pixels
Screen Size:	24"
Color Depth:	24 bit
Brightness:	300 cd/m^2 minimum
Contrast Ratio:	500:1 minimum

Other hardware and software you need:

- Windows workstation with an Internet connection.
- Internet browser (Internet Explorer, Firefox, or equivalent).
- The address (URL) of the Spectrum server so that you can log into Spectrum. (See the Spectrum administrator or your IT group for this address.)
- Aperio's ImageScope digital slide viewer. (If ImageScope has not been installed on your workstation, see the Spectrum administrator for assistance.) The version of Spectrum installed must be compatible with the version of Spectrum.
- Adobe Acrobat Reader (free download from www.adobe.com).

Personal Setup

Your Spectrum administrator sets up Spectrum for your institution's Digital IHC workflow. (These setup steps are covered in the *Digital IHC Guide to Spectrum Setup.)*

Each pathologist may also want to do a small amount of setup, discussed below. This setup only needs to be done once.

Select Your Spectrum Start Page

You can set up your Spectrum start page when you log in the first time into Spectrum (see "Instant Access, Anytime, Anywhere – Logging into Spectrum" on page 23 for details).

1. Go to the Spectrum Administrative menu and select **My Settings**.
2. In the **User Details** section, select the startup page you want to see when you log in by selecting the page from the **Spectrum Start Page** drop-down list.

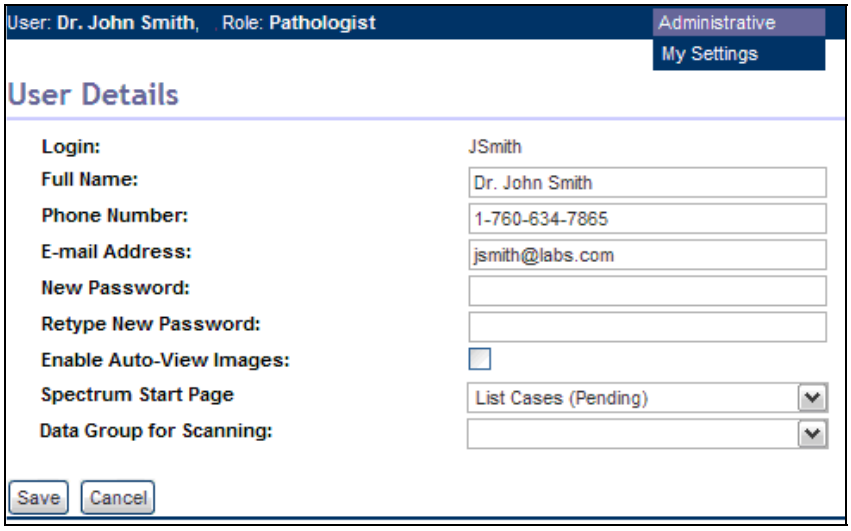
   We provide work lists based on case statuses that you can select as your Spectrum start page. Your Spectrum administrator can set up

The set up of Spectrum for your institution's Digital IHC workflow is discussed in details in the *Digital IHC Guide to Spectrum Setup*.

appropriate case statuses for your workflow. Work lists are automatically created for each case status and can be accessed via the Cases menu at the top of the Spectrum page as well as assigned as your start page.

Pathologists may want to go directly to the cases that need their attention. In our example, cases that need the attention from pathologists have the case status Pending and you would select **List Cases (Pending)**.

3. Click **Save** to save your settings.



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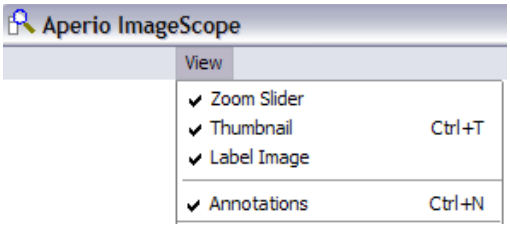
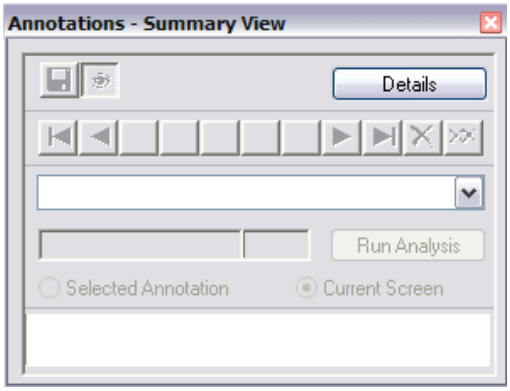
Set ImageScope Viewing Preferences

You can set up your ImageScope viewing preferences the first time you open a digital slide with ImageScope (see "Opening a Digital Slide" on page 25 for details).

1. Go to the ImageScope **View** menu and select your preferred viewing options. We recommend you select the following options.



2. If the Annotations window comes up in the Detailed View, click **Summary** to get the Annotations – Summary View that is used for the Digital IHC solution. You can move this window around so it is not in your way for viewing digital slides. A convenient location may be the bottom left corner in ImageScope.

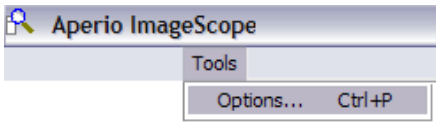


Set these viewing preferences on each computer you are going to use.

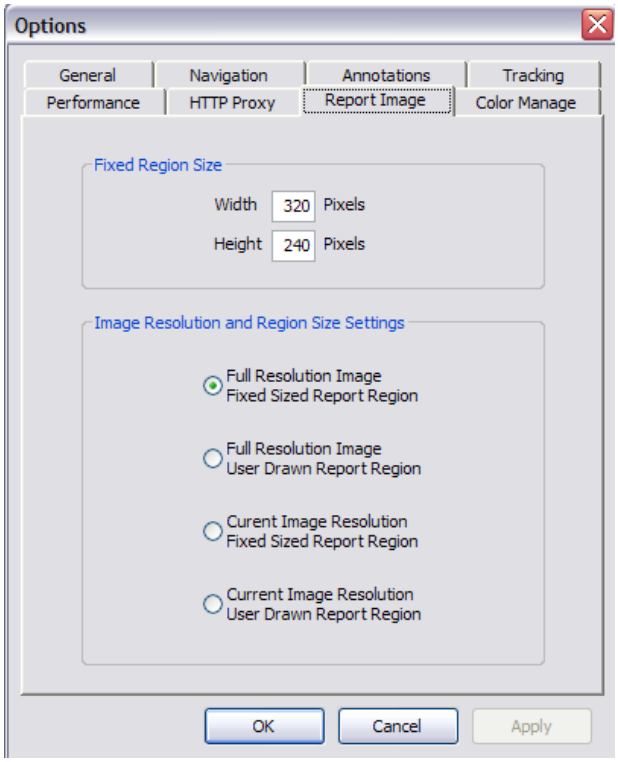
Set Report Image Preferences

You can set up your report image preferences the first time you open a digital slide with ImageScope (see "Opening a Digital Slide" on page 25 for details).

1. Go to the ImageScope Tools menu and select **Options…**.



2. Click the Report Image tab on the Options window. You can now select the image resolution and region size setting for the report image. Ask your Spectrum administrator which settings will work best with your report templates. For our IHC report template, we recommend that you select **Full Resolution Image, Fixed Sized Report Region** with a Width of 320 Pixels and a Height of 240 Pixels. Click **OK** to save your settings.

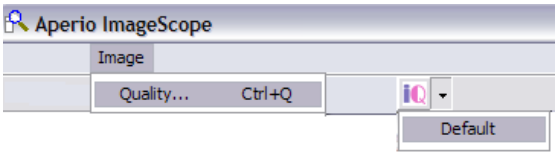


Set these report image preferences on each computer you are going to use.

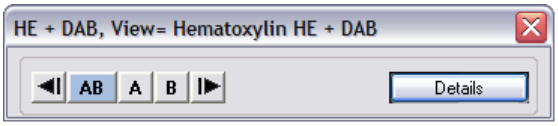
Set up Viewing Separate Stains (Optional)

You can set up your standard stain sets for your IHC slides the first time you open any digital slide in ImageScope (see "Opening a Digital Slide" on page 25 for details).

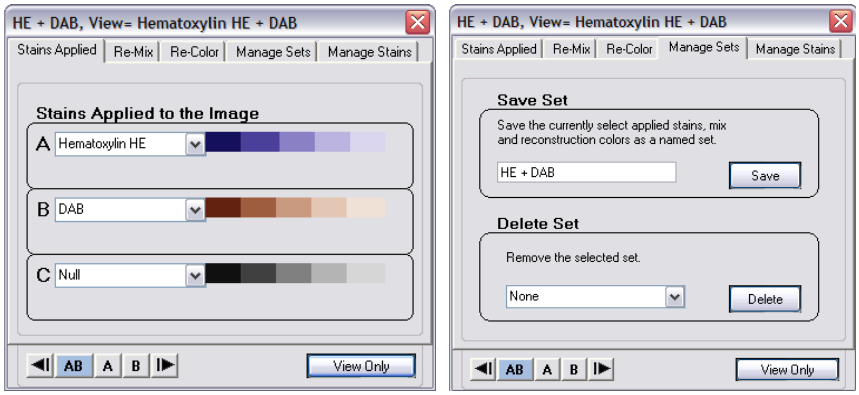
1. Click the IQ icon on the ImageScope toolbar and select the **Default** setting.
2. Go to the ImageScope Image menu and select **Quality ….**



You now see the IQ viewer toolbar.



3. Click the **Details** button on the IQ viewer toolbar.
4. Click the Stains Applied tab and select the stains used for your IHC slides, typically Hematoxylin and DAB.
5. To save this combination for future use, click the Manage Sets tab and type a name, like **HE + DAB** and click **Save**.



6. Click the **View Only** button on the IQ viewer toolbar.
7. Close the IQ viewer toolbar by clicking at the top of the window.

Create a stain set for each type of IHC digital slide you are going to view on each computer you are going to use to view digital slides.

From now on, when using IQ to view separate stains, you will be able to easily select the appropriate stain set for the digital slide you are viewing.

Instant Access, Anytime, Anywhere

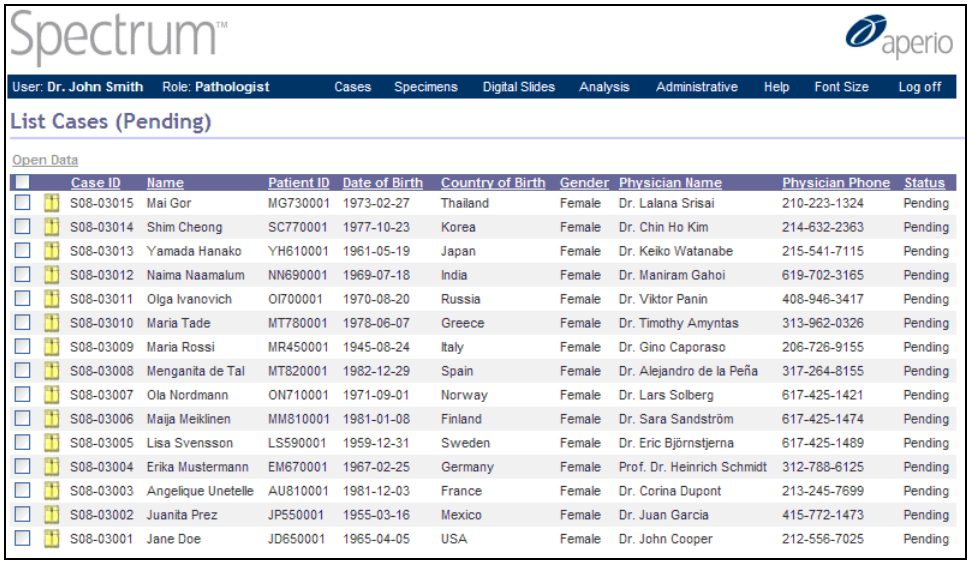
All digital pathology data is accessed via Aperio's web-based information management system, Spectrum. You can log into Spectrum—securely, anytime, anywhere—and read your cases as soon as they have been scanned.

Ask your Spectrum administrator for the Spectrum web address (URL), and for your username and password.

1. Open Microsoft Internet Explorer (or any other standard web viewer like Firefox) and enter the Spectrum web address. Spectrum displays the login page. (You may want to bookmark this web page for convenience.)
2. Log into Spectrum by entering your username and password and clicking the **User Login** button. You may be asked to change the password before continuing, depending on the security settings your Spectrum administrator has chosen for your account.

Case Management

We provide work lists based on case statuses so that every user of the system can manage his work efficiently. If you have set up your start page (see "Select Your Spectrum Start Page" on page 18) to be the list of cases that need your attention, you will see this list as soon as you log in. In our example, cases that need the attention from pathologists have the case status Pending.

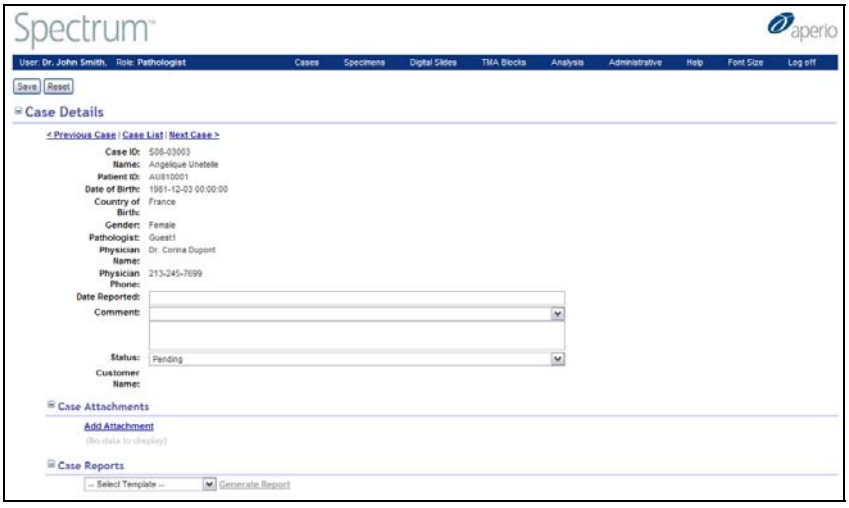

Spectrum
aperio
User: Dr. John Smith Role: Pathologist Cases Specimens Digital Slides Analysis Administrative Help Font Size Log off
List Cases (Pending)
Open Data

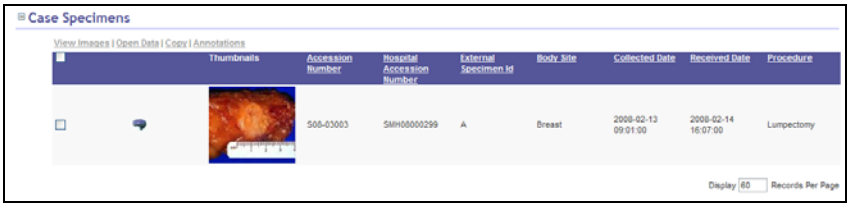
Case ID	Name	Patient ID	Date of Birth	Country of Birth	Gender	Physician Name	Physician Phone	Status
S08-03015	Mai Gor	MG730001	1973-02-27	Thailand	Female	Dr. Lalana Srisai	210-223-1324	Pending
S08-03014	Shim Cheong	SC770001	1977-10-23	Korea	Female	Dr. Chin Ho Kim	214-632-2363	Pending
S08-03013	Yamada Hanako	YH610001	1961-05-19	Japan	Female	Dr. Keiko Watanabe	215-541-7115	Pending
S08-03012	Naima Naamalum	NN690001	1969-07-18	India	Female	Dr. Maniram Gahoi	619-702-3165	Pending
S08-03011	Olga Ivanovich	OI700001	1970-08-20	Russia	Female	Dr. Viktor Panin	408-946-3417	Pending
S08-03010	Maria Tade	MT780001	1978-06-07	Greece	Female	Dr. Timothy Amyntas	313-962-0326	Pending
S08-03009	Maria Rossi	MR450001	1945-08-24	Italy	Female	Dr. Gino Caporaso	206-726-9155	Pending
S08-03008	Menganita de Tal	MT820001	1982-12-29	Spain	Female	Dr. Alejandro de la Peña	317-264-8155	Pending
S08-03007	Ola Nordmann	ON710001	1971-09-01	Norway	Female	Dr. Lars Solberg	617-425-1421	Pending
S08-03006	Maija Meiklinen	MM810001	1981-01-08	Finland	Female	Dr. Sara Sandström	617-425-1474	Pending
S08-03005	Lisa Svensson	LS590001	1959-12-31	Sweden	Female	Dr. Eric Björnstjerna	617-425-1489	Pending
S08-03004	Erika Mustermann	EM670001	1967-02-25	Germany	Female	Prof. Dr. Heinrich Schmidt	312-788-6125	Pending
S08-03003	Angelique Unetelle	AU810001	1981-12-03	France	Female	Dr. Corina Dupont	213-245-7699	Pending
S08-03002	Juanita Prez	JP550001	1955-03-16	Mexico	Female	Dr. Juan Garcia	415-772-1473	Pending
S08-03001	Jane Doe	JD650001	1965-04-05	USA	Female	Dr. John Cooper	212-556-7025	Pending

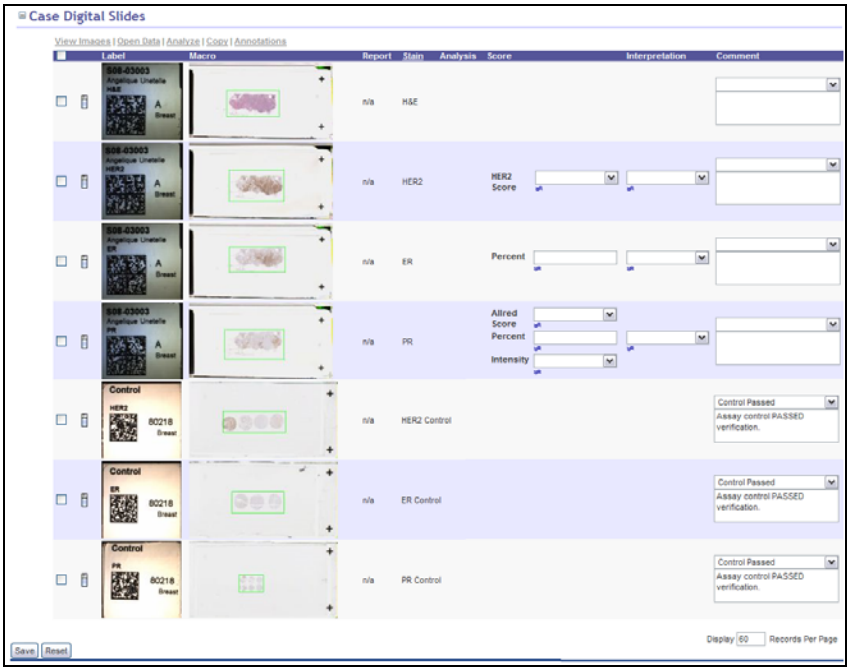
View all Case, Specimen and Slide Information

When you open a case, all case, specimen and slide information, including gross images and controls, are conveniently at your fingertips.

3. On the case list, open the case to be reviewed by clicking on the open data icon for the case. The Case Details page opens for that case.







Reading Slides on a Computer Monitor

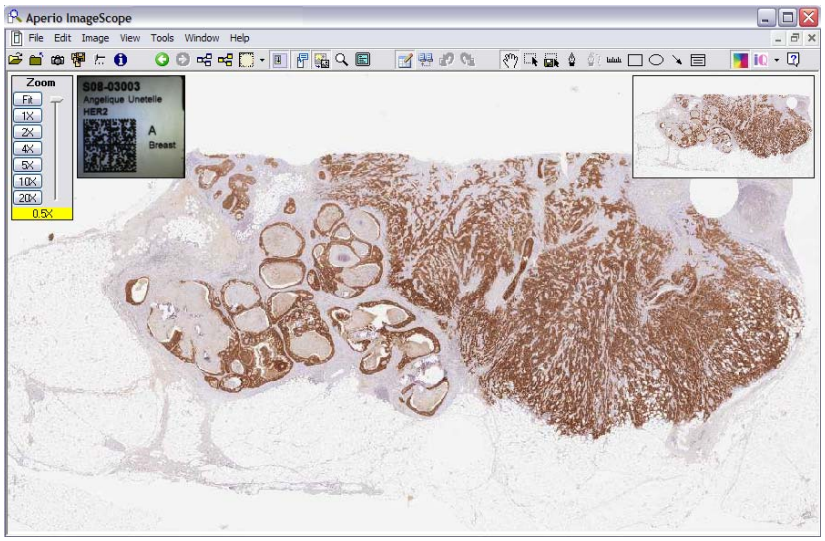
Please refer to the Digital IHC application guides for more details (including intended use) on the reading of IHC slides on a computer monitor.

Open

On the case page, scroll down to the Case Digital Slides list to see the slides associated with this case.

4. To quickly open a slide in ImageScope, click on the thumbnail of the Macro image. To open multiple slides simultaneously, select the check box next to all slides you want to open and click **View Images**.

The slide appears in the ImageScope window.



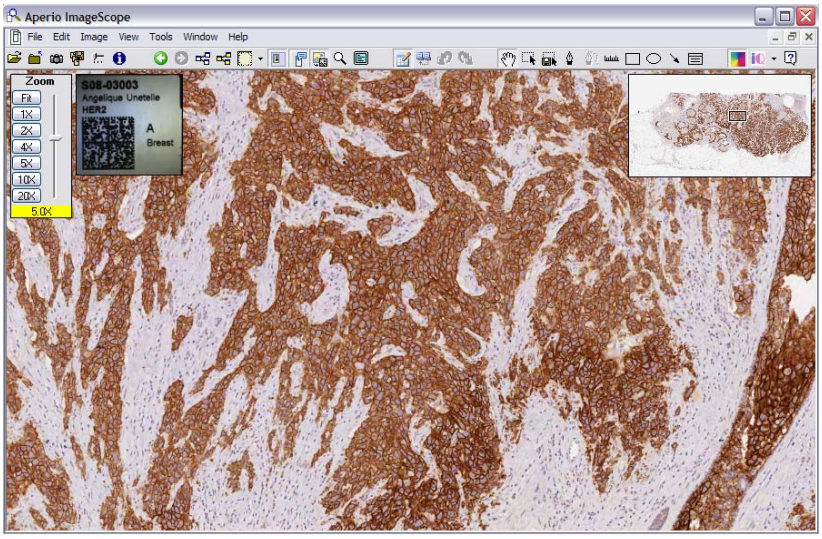
For more detailed information on how to view slides, please refer to the *ImageScope User's Guide*.

Navigate

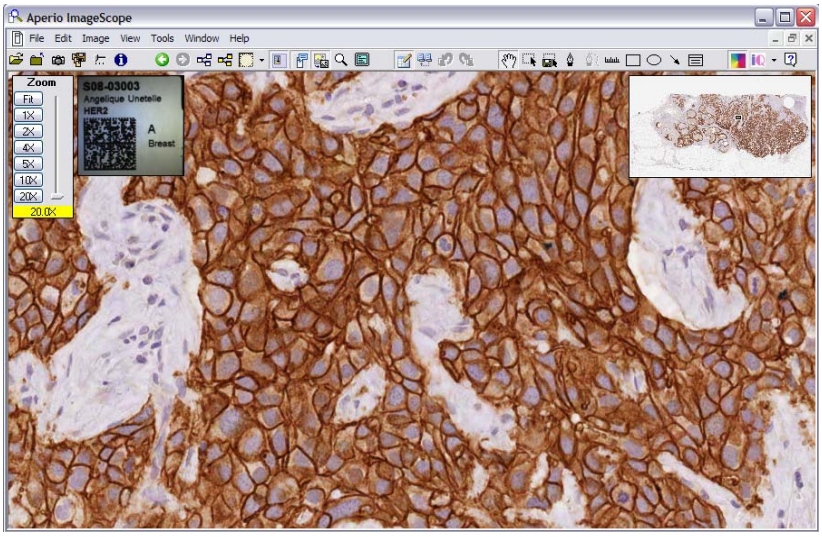
To read a slide you need to navigate through the slide in much the same way you would with a microscope. You can pan and zoom, but do not need to focus. The image of the tissue is already in focus (optimum focus has been determined during the scanning of the slide).

You may want to start at a low-power of 4x or 5x that provides you with diagnostic viewing capabilities and pan through the slide to look for invasive tumor regions. When you identify an invasive tumor region, you can then go to the highest-power and do your quantitative assessment. Then go back to low-power and continue scanning the slide for more invasive tumor regions.

5. Click **5X** on the zoom slider.



6. Pan through the slide by clicking on the slide, holding and moving.
7. Zoom in by double-clicking on the invasive tumor regions.



8. Zoom out by double-clicking again and continue panning.

Here is a short list of common zooming and panning features in ImageScope (commands in *italic* are preferred for fast, single-hand operation):

Zoom: Adjust zoom level by using the controls in the zoom slider—Fit, 1x, …20x.

Increase and decrease zoom by rolling the mouse wheel: toward you (zoom in) and away from you (zoom out). First, click anywhere on the digital slide to enable this mode. If you accidentally click the wheel, you start a panning mode not described here—just click anywhere on the slide to return to the normal mode.

Go to maximum zoom level (highest resolution) by double-clicking any location of the digital slide. Go back to the previous zoom level by double-clicking again.

Pan: Position the slide view by clicking on the rectangle (current view) in the slide thumbnail window, holding and moving to the desired position.

Move the view by clicking on the slide, holding, and moving.

Move to an adjacent view by pressing the Shift and arrow-up, -down, -left, and -right keys.

Slide Quality Control

It is up to the pathologist to verify that the slides are of sufficient quality to perform his/her task, whether that is a manual read of the digital slide or image analysis.

Note that the quality of a slide depends on the laboratory following the quality control instructions recommended in the labeling of IHC assays. It is recommended that the pathologist follows the appropriate instructions in the specific IHC assay to assess the quality of the slide preparation.

The pathologist should review the quality of the scanning by evaluating that the entire tissue sample has been scanned and that the tissue is in focus.

The staining process can yield artifacts that need to be assessed properly by the pathologists. Typical artifacts to consider are: normal epithelium staining, heterogeneous staining, background staining, and cytoplasmic background staining as well as edge, thermal and crush artifacts. Staining artifacts should be considered carefully. In some cases, severe staining artifacts may prevent accurate IHC image analysis. Those regions should be excluded from the IHC image analysis.

IHC image analysis is sensitive to excessive cytoplasmic staining and tissue being out of focus. It is the responsibility of the pathologist to know the limitations of the algorithm and to make sure that only good quality digital slides are used for the IHC image analysis.

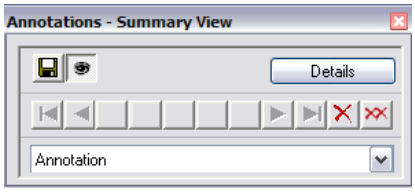
If slides have poor quality, it might be necessary to prepare a new slide or to re-scan the slide.

- **The pathologist verifies that the entire tissue sample has been scanned and requests a re-scan of the slide if the scan area does not include the entire tissue sample.**
- **The pathologist assesses the presence of any staining artifacts, in particular cytoplasmic staining, and requests the preparation of a new slide if excessive cytoplasmic staining is observed.**
- **The pathologist assesses the focus of the digital slide and requests a re-scan of the slide if the tissue in the tumor regions is out of focus.**

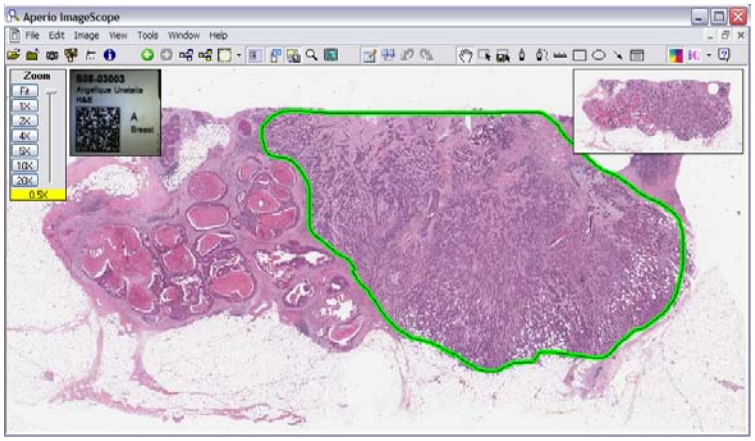
Annotate Tumor Regions on H&E Slides (Optional)

You typically read the H&E slides first to determine the need for an IHC Panel. You could annotate the invasive tumor regions on the digital H&E slides to help you find them faster and more reliably later when you are reading the IHC slides. You can use the annotation tools in ImageScope to mark the invasive tumor regions.

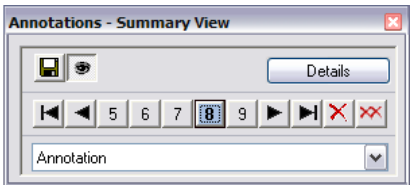
9. If you want to provide any form of annotations, first select **Annotation** in the Annotations drop-down list on the Annotations window.



10. Then click on the Pen icon on the ImageScope toolbar and draw an outline of the invasive tumor region. Regions can be outlined anywhere in the slide and at any zoom level. Note that the drawing tools are not persistent—for each region to be outlined, you must select the drawing tool again and then outline the region. To delete any region, click the annotation on the main ImageScope window to select it and press the Delete key on your keyboard.



11. You can easily navigate from one annotation to the next by clicking on the corresponding region numbers in the Annotations window.



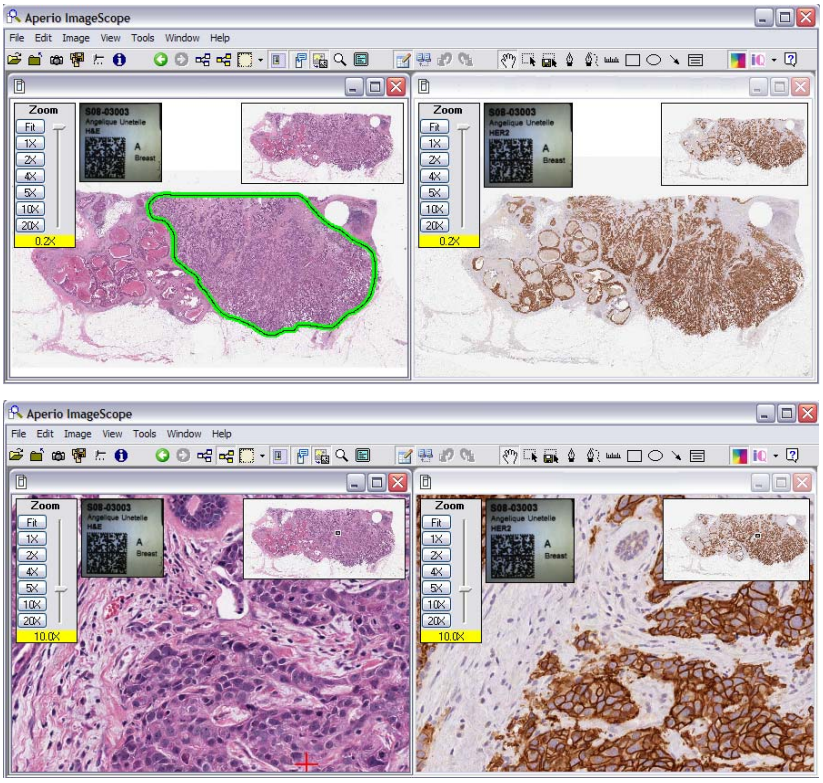
When you outline the tumor regions on the H&E slides, your lab could provide a service where it pre-identifies the tumor regions on the IHC slides and pre-runs image analysis for you based on the tumor regions you outlined.

View H&E and IHC Slides Side-by-Side (Optional)

Something you cannot do on a microscope is to view multiple slides side-by-side. You know how difficult it can be to identify invasive tumor regions on a negative IHC slide. Being able to view the H&E and IHC slides side-by-side can help you to identify the tumor regions faster and more reliably.

Using advanced computer technologies, multiple slides can be automatically synchronized so that when you navigate through one of the slides you see the same region at the same magnification in all slides.

12. Click the smart synchronization icon on the ImageScope toolbar to automatically synchronize all open slides. (Note that this icon is similar to the manual synchronization icon, , except that it is yellow instead of white.)



If smart synchronization is not effective because of special tissue characteristics such as torn or missing tissue, then you can use manual synchronization. Set all slides to the same magnification, align them manually, and then click the manual synchronization icon .

IQ offers many more features than simply viewing separate stains, such as adjusting stain colors to your preference or standards, measuring your stains, and so on—see the *IQ Image Quality User's Guide* for details.

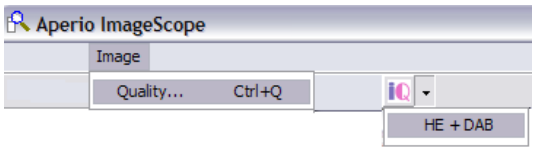
Use IQ to View Separate Stains (Optional)

With nuclear stains, like ER or PR, it may be challenging to identify faint DAB staining on the nuclei, as Hematoxylin (the background staining) and DAB colocalize on the nuclei.

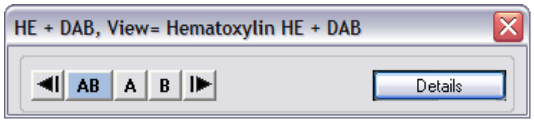
Using advanced computer technologies, the stains can be properly separated and you can look at the individual stains. This way you can easily identify faint DAB stained nuclei as well as any positive stained region on the slide (hot spots).

13. Click the IQ icon on the ImageScope toolbar to select the appropriate stain set, such as **HE + DAB,** from the IQ drop-down list. Make sure to set up the stain sets for your IHC slides (see "Set up Viewing Separate Stains (Optional)" on page 22).

14. Go to the ImageScope Image menu and select **Quality…**.

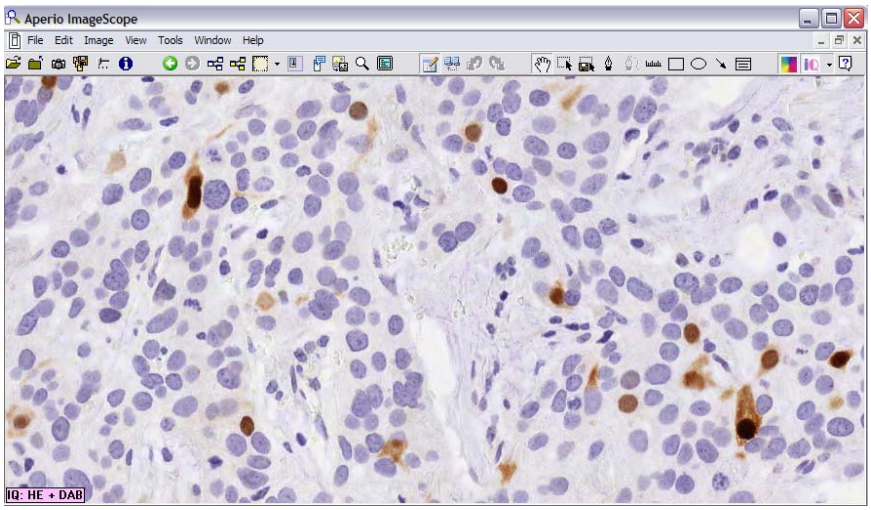


You see the IQ viewer toolbar.

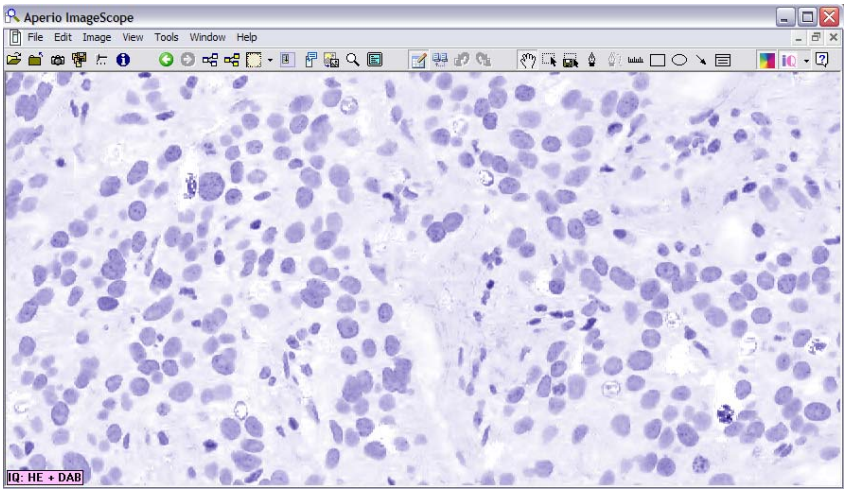


15. Use the IQ viewer toolbar to view separate stain channels:

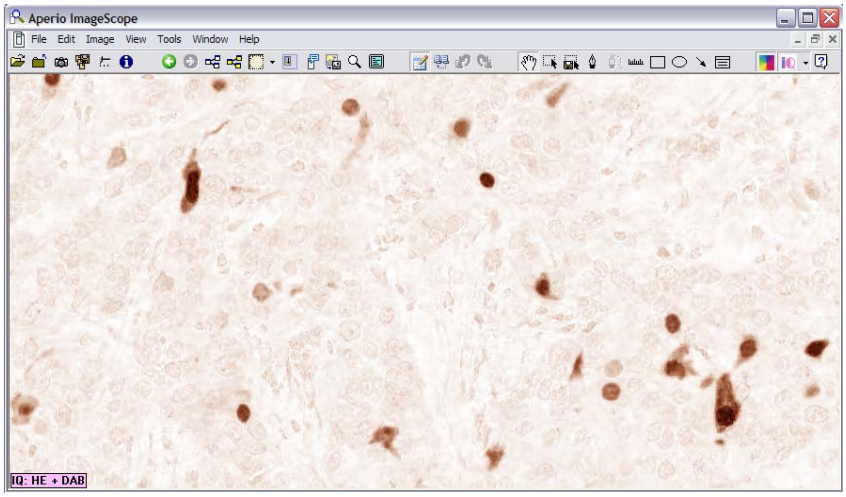
AB to see both stains at the same time:

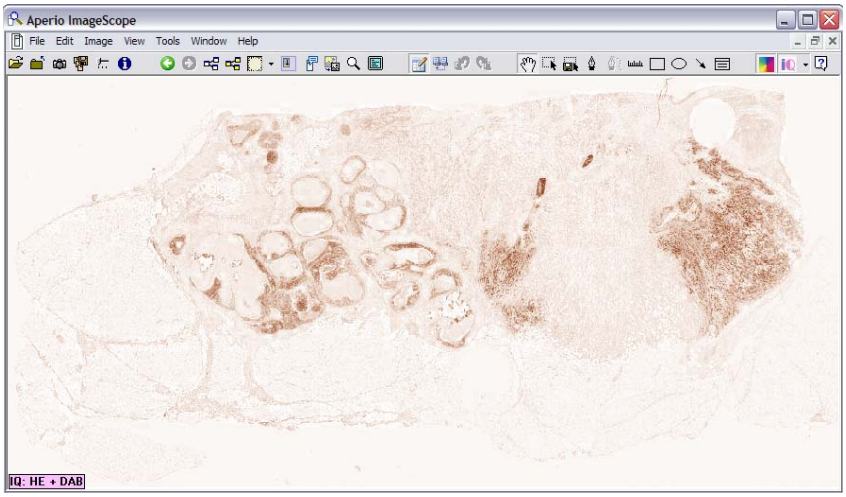


A to see the first stain only (in this example, Hematoxylin):



B to see the second stain only (in this example, DAB)





16. Click ✕ at the top of the IQ viewer toolbar to turn off IQ.

Run Image Analysis

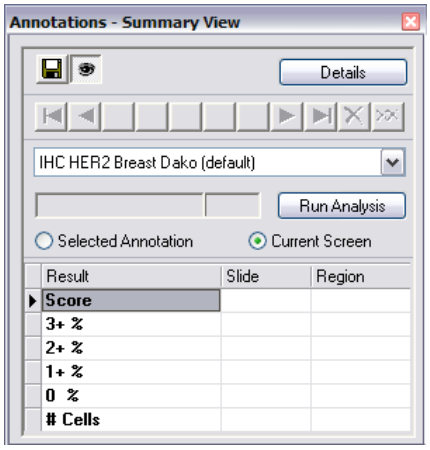
Aperio provides a new approach to IHC with an all-digital solution. While reading slides on a computer monitor you can now use quantitative image analysis efficiently with a simple click of a button. Image analysis classifies and counts thousands of cells for you accurately and consistently in just seconds.

The entire slide is important for assessing the tumor and Aperio's Digital IHC solution makes the entire digital slide available to you for image analysis.

When identifying tumor regions for analysis, make sure to properly identify invasive cancer versus carcinoma-in-situ and not to include regions with staining artifacts. If the staining is heterogonous, ensure that your choice of tumor regions for analysis is representative for the heterogeneity of the tumor.

When you have identified an invasive tumor region you want to use for quantitative image analysis, the easiest way is to run analysis on the current screen. Make sure to zoom in to the highest magnification when running analysis to keep the processing time short.

17. Click **Run Analysis** on the Annotations window. If the Annotations window is not shown, go to the View menu in ImageScope and select **Annotations** or press the Ctrl and N keys.

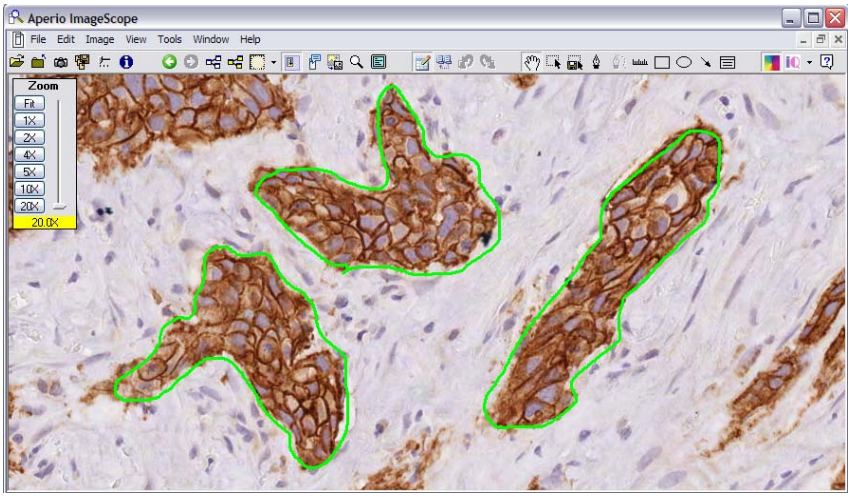


The appropriate algorithm for the analysis, identified as "(default)," is automatically selected for you. For advanced users: You may run any other analysis algorithm available to you as well, but only the results from the default algorithm will be available in Spectrum for further reporting.

Some of our algorithms provide an automatic tumor cell detection capability that identifies tumor cells (versus lymphocyte, stroma and normal cells) and only includes those tumor cells in the analysis. This capability provides robust analysis results when the analysis is run on the entire screen or on coarse tumor regions that not only include tumor cells but also lymphocyte, stroma and normal cells. Consult the Digital IHC application guides to learn more about the capabilities of the algorithms you are using.

Other algorithms provide only a limited capability to identify tumor cells and you are required to identify the tumor cell-only regions (excluding lymphocyte, stroma and normal cells) for the analysis.

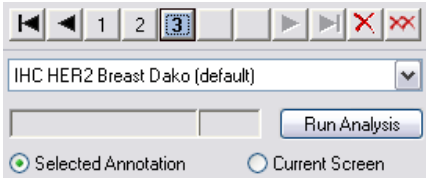
17a Click on the Pen icon on the ImageScope toolbar or simply press F2 and draw an outline of the invasive tumor region. Alternatively, you can use the rectangle drawing tool by clicking on the Rectangle icon or pressing F5. Regions can be outlined anywhere in the slide and at any magnification (images are always analyzed at the maximum resolution of 20x). Note that the drawing tools are not persistent—for each region to be outlined, you must select the drawing tool again and then outline the region. Note as well that if you interrupt the drawing of a region, ImageScope will close the region by connecting the end points (not visible). If this is not what you want, then you should delete the current outlined region by pressing the Delete key and starting over again with this region. Once you draw a region, a numbered button that corresponds to the region you have drawn shows up the Annotations window.



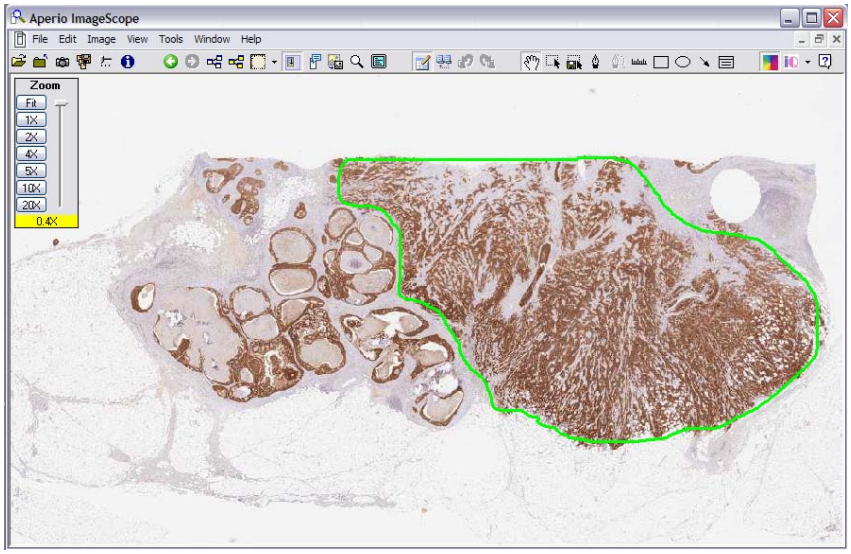
Note that when you want to outline regions for analysis that the appropriate algorithm name needs to be selected in the annotations window, not **Annotations**—Annotations are for general annotations of the slide.

The default setting for the analysis of Current Screen is automatically changed to Selected Annotation when you outline regions for analysis. You can outline as many regions as you like and then run analyses on them.

17b Click **Run Analysis** on the Annotations – Summary View window. If the Annotations window is not shown, go to the View menu in ImageScope and select **Annotations** or press the Ctrl and N keys.



You can also analyze the entire invasive tumor by using an algorithm with automatic tumor cell detection and running it on a coarse outline of the invasive tumor regions. Processing those large regions may take some time and a different workflow is recommended to save you time where the lab pre-runs image analysis for you based on the tumor regions you outlined on the H&E slide.

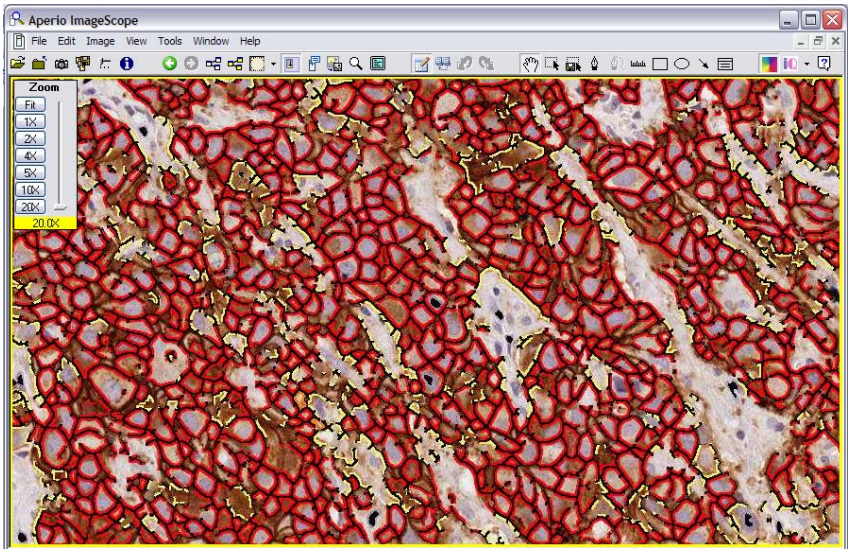


Digital slides consist of large images and the analysis of large images requires considerable processing resources. Aperio provides server-side processing for its image analysis so that the images are processed where they reside, thereby eliminating the need for moving the images over the network and also not using the processing resources on the pathologist's computer. Aperio's server-side analysis also provides a scaleable processing architecture that allows easily adding computer resources to the server to meet expanding analysis needs to guarantee fast response times for a large number of users and allows the image analysis to keep up with slide scanning.

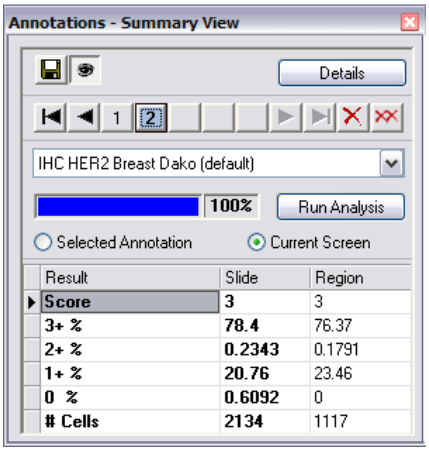
While analyzing, a progress bar is shown in the Annotations window. It should take about 6 seconds to analyze the current screen at 20x (about 2,000 to 3,000 cells).

Once the analysis is complete, a mark-up image of the individual cell classifications can be seen in the ImageScope window and the numerical results of the analysis can be reviewed in the Annotations window.

The mark-up image highlights the detected cells which are color-coded according to their classification (blue = 0, yellow = 1+, orange = 2+, red = 3+). The markup image allows you to easily verify the analysis results and to gain confidence in using this new technology. You can view the digital slide with or without the mark-up image by clicking on the eye icon (without) (with mark-up image) in the Annotations window.

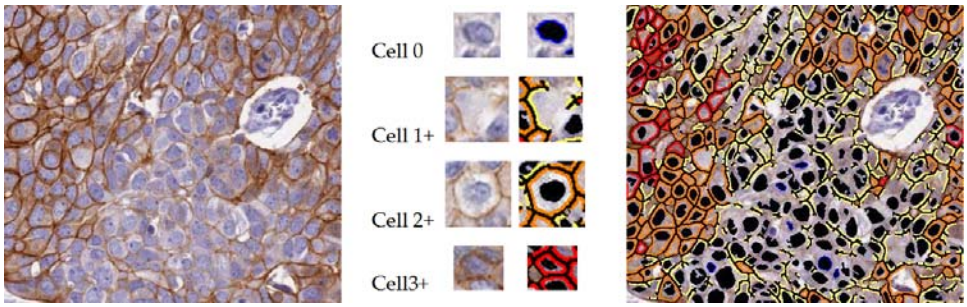


The analysis results provide the number of detected cells, the percentage of cells per class (0, 1+, 2+ and 3+) corresponding to the mark-up image and the assay specific scores (e.g., HER2 score for HER2, and Percentage and Intensity Score for ER/PR). The analysis results are provided for each region and accumulated for the entire slide (all regions).



HER2

The HER2 image analysis detects the membrane staining for the individual tumor cells and quantifies the intensity and completeness of the membrane staining. Tumor cells are individually classified as 0, 1+, 2+ and 3+. A tumor cell is classified 0 when there is no membrane staining, 1+ when there is only partial membrane staining or weak membrane staining, 2+ when there is moderate and complete membrane staining, and 3+ when there is intense and complete membrane staining.



Score	2
3+ %	7.0
2+ %	30.0
1+ %	61.0
0 %	2.0

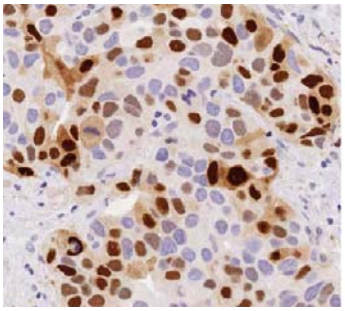
Based on the percentages of 0, 1+, 2+ and 3+ classified cell scores, a HER2 assay Score of 0, 1+, 2+ or 3+ is determined. The score is 3+ if more than 10% of the cells are stained at the 3+ level, 2+ if more than 10% of the cells are stained at the 2+ and higher levels, 1+ if more than 10% of the cells are stained at the 1+ and higher level, and 0 if less than 10% of the cells are stained at the 1+ or higher levels.

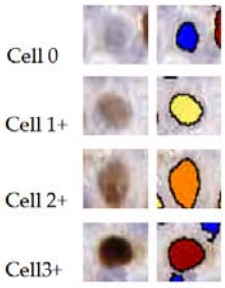
As you can see, the HER2 image analysis not only provides the coarse HER2 score but also a detailed breakdown by percentages of 3+, 2+ and 1+ cells that allows you to identify border line cases easily and use our HER2 image analysis readily with the new CAP/ASCO HER2 guidelines. Your Spectrum administrator can set up an automatic HER2 score calculator as part of Spectrum that uses the 30% threshold for 3+ cells as outlined in the CAP/ASCO HER2 guidelines.

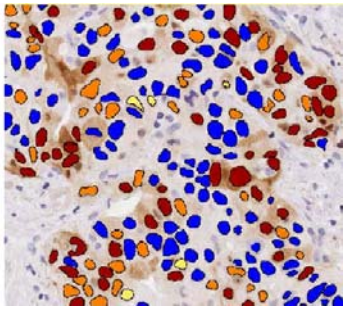
Please refer to the Digital IHC application guides for more details on the image analysis application you are using for HER2.

ER/PR

The ER/PR image analysis detects the positive nuclear staining for the individual tumor cells and quantifies their staining intensity. Cells (Nuclei) are individually classified as 0, 1+, 2+ and 3+. A nucleus is classified 0 when it has no nuclear staining, 1+ when it has weak nuclear staining, 2+ when it has moderate nuclear staining, and 3+ when it has intense nuclear staining.







Percent	52.3
Intensity	3
3+ %	28.5
2+ %	21.3
1+ %	2.5
0 %	47.7

Based on the percentages of 0, 1+, 2+ and 3+ cells, the percentage of positive stained cells as a percentage of 0 to 100% and the average staining intensity of the positive nuclei as a score of 0, 1+, 2+ or 3+ is determined.

Cytoplasmic or background staining can create problems for the correct quantization of the staining because it increases the overall staining intensity of the slide. Cytoplasmic or background staining can also create problems for image analysis algorithms because segmentation of the nuclei becomes more difficult. Slides that exhibit high cytoplasmic or background staining due to the staining process (vs. biological cause) should be caught by the laboratory's quality control process. In any case, our ER/PR image analysis is able to deal with a certain degree of cytoplasmic or background staining. The ER/PR image analysis detects cytoplasmic staining and corrects for it in the staining intensities and in the segmentation of the nuclei.

An interesting point about ER and PR scoring is that many labs use different scoring schemes—some use the percentage of positive cells with a 1%, 5% or 10% cut-off, some use the Allred score, and others have their own scoring scheme combining intensity and percentage to derive a meaningful score. Our ER/PR image analysis provides the percentage of positive cells and the intensity score on which all those scoring schemes are based. Your Spectrum administrator can set up an automatic score calculator as part of Spectrum that implements the scoring scheme established in your institution.

Please refer to the Digital IHC application guides for more details on the image analysis application you are using for ER/PR.

At this point, you can add regions and run analyses again.

The IHC image analysis works incrementally, which means that as you add new regions and click **Run Analysis** on the Annotations window, only the new regions are analyzed. Any time you click **Run Analysis** again, all slide results are updated.

As you add regions, additional numbered buttons appear on the Annotations window. You can easily navigate between regions by clicking on the numbered button corresponding to a region or use the arrow keys to step through them all. The selected region is shown centered in the ImageScope window.

To delete any region, click the annotation on the main ImageScope window to select it and press the Delete key on your keyboard, or select the numbered button for the region in the Annotations window and click the icon.

When you delete an analyzed region, the slide results are automatically updated.

Image Analysis Quality Control

IHC image analysis is an aid to the pathologists. It is the responsibility of the pathologists to verify the proper operation of the analysis.

It is important that the pathologists feel comfortable with the IHC image analysis but identify when it might have failed (quality control). Aperio's IHC image analysis makes it easy for the pathologists to follow what the analysis is doing and how scores were determined. The analysis provides meaningful outputs of the different processing steps to which the pathologist can relate intuitively, the same cell features, and the same scoring scheme as used for manual scoring.

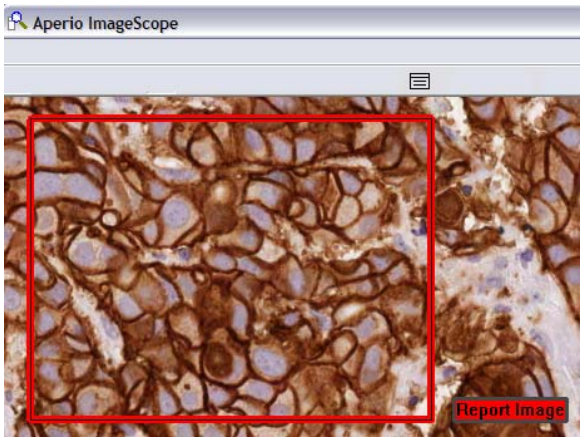
- **The pathologist reviews the mark-up image for each of the tumor regions and makes sure that the analysis properly detected and classified the tumor cells.**

If there are regions where the analysis did not perform properly, then those regions need to be excluded from the analysis. Deleting regions may require adding new regions to make sure that the tumor regions used for the analysis are representative for the tumor. If it is impossible to analyze a representative set of tumor regions where the algorithm performs properly, then the IHC image analysis should not be used for this particular slide.

Select Report Image

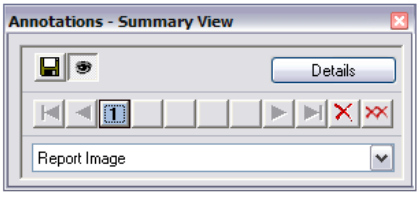
With a simple click of a button you can designate a representative region of the slide that will be automatically included in your report.

18. Click the Report Region Tool icon on the ImageScope toolbar and then click the area of the image that you want to appear in your report.



Only one report image can be selected for a slide, and a report image only appears in a report if the report template used has the provision for using report images.

Later on you can navigate to the report image region by selecting **Report Image** in the Annotations window. To go back to the analysis, you need to reselect the appropriate image analysis algorithm that is marked **(default)** in the Annotations window.



Close

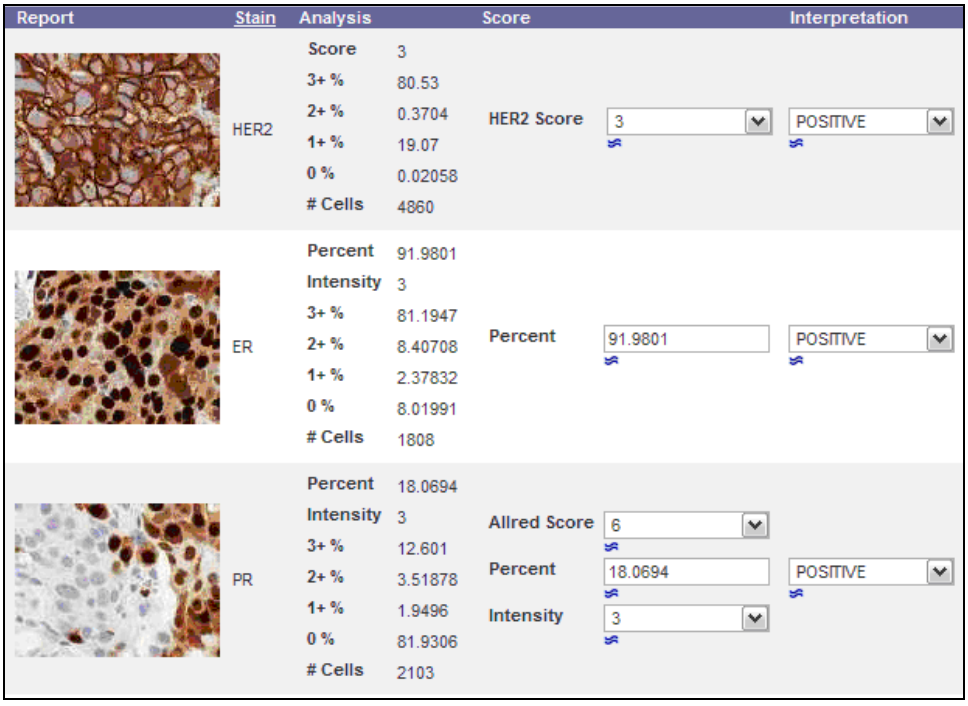
Once you read the IHC slide, run image analysis and designate a report image, you need to save all annotations and close ImageScope.

19. Click the **Save** icon in the Annotations window.
20. Click at the top of the ImageScope window.

Automatic Data Flow from Analysis to Reports

Aperio automates the data flow from analysis to reports for you, providing automatic score and interpretation calculation.

It is the responsibility of the pathologist to provide the final score based on his/her assessment. If you agree with the provided scores and interpretation, you do not need to do anything. If you disagree, just overwrite the score or interpretation results in question. Values that have been updated automatically are shown with a link icon. Overwritten values are shown with a broken link icon. Once a value has been overwritten, it is no longer updated automatically, making sure that data provided by the pathologists always takes precedence.



Spectrum shows for each slide the Report image, the Analysis results, as well as the Score and the Interpretation results. Your Spectrum administrator can set up the slide-specific processing for each slide, defining the appropriate image analysis algorithm and the specific score and interpretation schemes that are used in your institution. The analysis results here are the same as the slide results in the Annotations window in ImageScope. Note that only the results from the specified image analysis algorithm (default) are reported here, making sure that the right analysis always is used. When the analysis results are updated in ImageScope, the results in Spectrum are also updated at the same time. Scores can be copied over directly from the analysis results and/or a new calculated score can be defined. Our automatic score calculator can be used to create any scoring scheme you want, such as a score that follows the new CAP/ASCO guidelines for HER2, the Allred Score or for that matter any score that is based on the percentage of positive cells and the intensity score for ER/PR, or the H-Score. The interpretation can be calculated automatically based on a score.

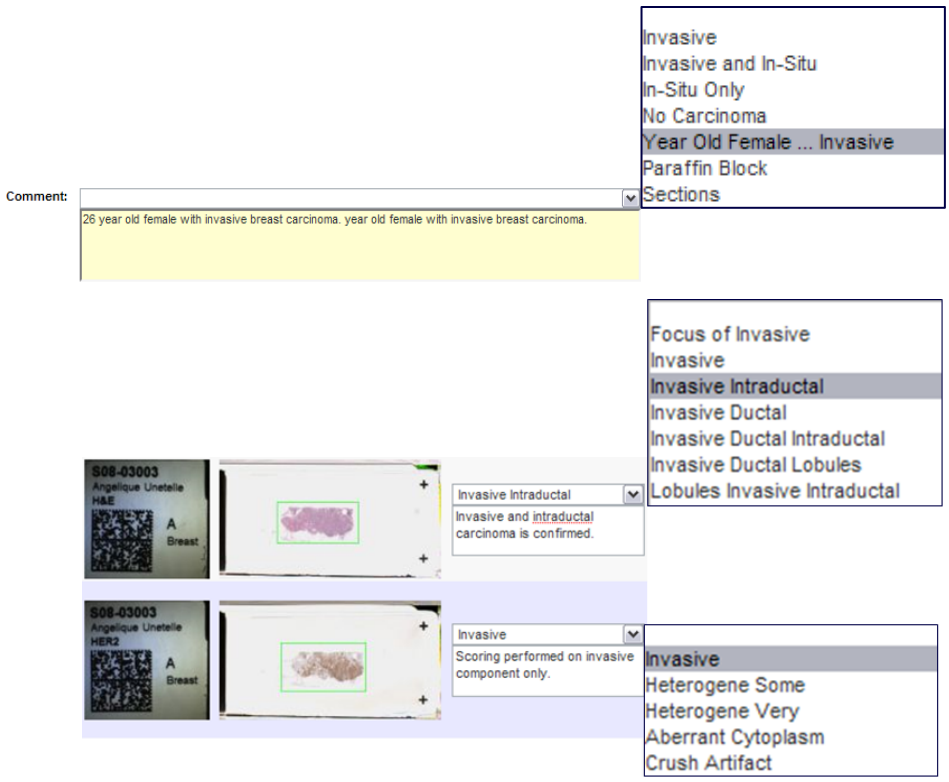
Generate Reports

Easy Data Entry using Canned Comments

The slide and case comments can be entered easily, accurately, and quickly using canned (pre-defined) comments.

21. Select a **canned comment** from the drop-down list of the slide and case comment fields. You can add any number of canned comments for a field, edit the canned comments you used, and add your own text.

Your Spectrum administrator can define the canned comments for your institution. Specific canned comments can be defined for your different slide types (e.g., Breast/H&E, HER2, ER, PR) and the case comment (see the *Digital IHC Guide to Spectrum Setup).*



Once you have entered all data, you need to save it. Note that all data fields that have been changed but have not yet been saved are colored yellow.

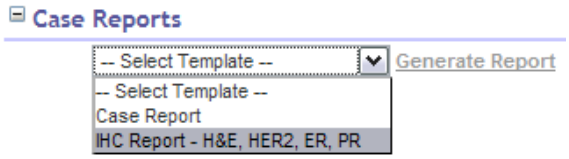
22. Click the **Save** button on the top or bottom of the Case page.

Automatic Report Generation

Automatically create error-free professional reports with representative images from the slides. You can now generate professional reports yourself while reviewing a case.

> For more information on creating reports, see the *Spectrum/Spectrum Plus Reporting User's Guide.*

23. Go to the Case Report section and select the appropriate report template from the drop-down list.
24. Click **Generate Report**.



It is easy to create a new report template tailored to your institution's needs. Any information in the database can be laid out in a professional report in exactly the format you desire. Ask your Spectrum administrator which report template you should use.

As you can see with our IHC HER2, ER, PR report template (next page), your customer or oncologist address with logo, your address with logo, patient information, case comment, specimen information and the scores, interpretation, comments and images of the slides are automatically pulled into a nicely laid out report. If image analysis was used on an IHC slide, this is clearly identified for your billing purposes.

Once you have reviewed the report you can use an electronic signature to sign it.

25. Click **Sign**.

26. Enter your Password (the password you used to log into Spectrum.) and click **Sign.**

FINAL Report	IHC REPORT	Report Date: February 15, 2008

THE Lab
1360 Park Center Dr.
Vista, CA 92081
Phone: 866-478-4111
Fax: 760-539-1116

Santa Maria Hospital
1 Main Street
Los Angeles, CA 90001
Phone: 213-245-7656
Fax: 212-245-7600

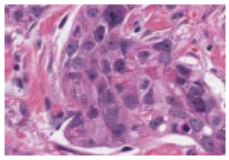
PATIENT	PATIENT ID	DOB	GENDER	AGE	PHYSICIAN	PHONE
Angelique Unetelle	AU810001	1981-12-03 00:00:00	Female	26	Dr. Corina Dupont	213-245-7699

CASE COMMENTS

26 year old female with invasive breast carcinoma.

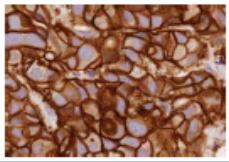
SPECIMEN

SPECIMEN ID	HOSPITAL ACCESSION	ACCESSION NUMBER	COLLECTED DATE	RECEIVED DATE	BODY SITE	PROCEDURE
A	SMH08000299	S08-03003	2008-02-13 09:01:00	2008-02-14 16:07:00	Breast	Lumpectomy



H&E

Invasive and intraductal carcinoma is confirmed.

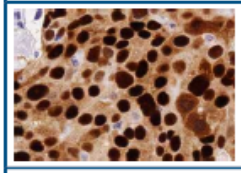


HER2 — **POSITIVE**

Score: 3

Used computer assisted image analysis

Scoring performed on invasive component only.

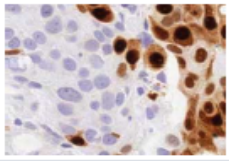


ER — **POSITIVE**

Score: 91.9801

Used computer assisted image analysis

Scoring performed on invasive component only.



PR — **POSITIVE**

Score: 6

Used computer assisted image analysis

Scoring performed on invasive component only.

Signature: Dr. John Smith - 1-760-634-7865	February 15, 2008	Page 1 of 2

This test was performed by IHC in conjunction with computer assisted image analysis where specified. The specimen is a section of formalin fixed and paraffin-embedded tissue.

The HER2/neu slide was stained with the HercepTest from DakoCytomation.

The ER slide was incubated with the 1D5 monoclonal anti-ER antibody from DakoCytomation at a 1:25 dilution for 30 minutes which was visualized with DAB. The slide was then counterstained with DakoCytomation hematoxylin for 1 minute.

The PR slide was incubated with the PgR636 monoclonal anti-PR antibody from DakoCytomation at a 1:100 dilution for 30 minutes which was visualized with DAB. The slide was then counterstained with DakoCytomation hematoxylin for 1 minute.

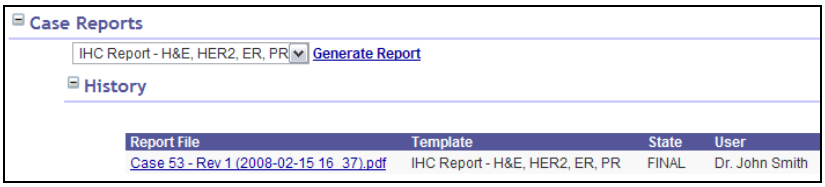
While some antibodies have not been approved by the FDA, clearance/approval is not mandated. These antibodies are well documented and clinically accepted prognostic indicators. Known positive and negative control tissue show appropriate staining. The prognostic marker results should be used in context with clinical/pathological findings.

Angelique Unetelle November 19, 2008 11:39 AM Page 2 of 2

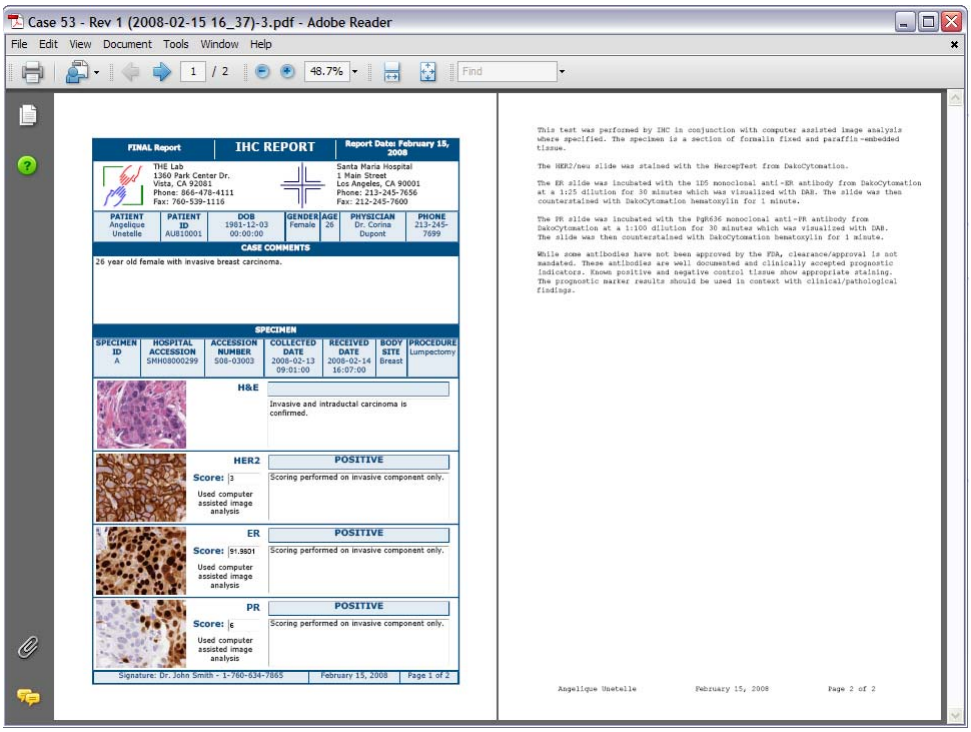
Sign Save Cancel

After signing, the report is automatically created in Adobe Acrobat format in a secure format that cannot be edited and it is stored at a secure server location.

27. Go to the History section under Case Reports and click on the Report File.



This will open the report in Adobe Reader. (You must have Adobe Acrobat Reader installed on your computer to view the report.)

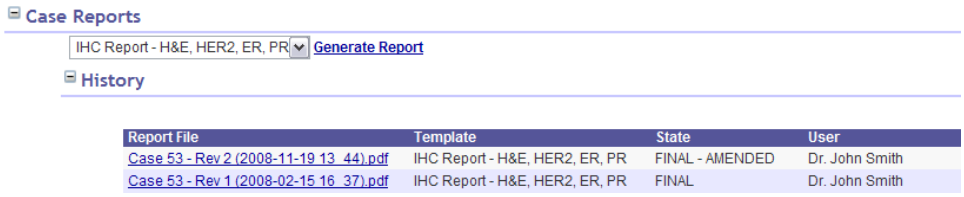


From within Adobe Reader you can then print, save or email the report.

Amendments and Corrections

Once a report has been signed, you have to amend or correct it if you need to modify it. First, make your changes and then generate the report again. Now before you can sign the report you need to specify if you want to do an Amendment or Correction by choosing from the Select Update Type drop-down list. Then you need to sign the report again using the electronic signature.

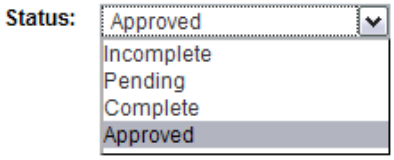
A new report is automatically created and can be found in the History section under Case Reports.



Finish the Case

When you are finished with the case, select the case status that your organization uses to identify reviewed cases.

28. Go to the Case Details section and select the new case status from the **Status** drop-down list.



Your Spectrum administrator can set up appropriate case statuses for your workflow. In our example, when a final report has been generated for a case, the new case status is **Approved**.

Now you can go to your next case.

29. Click **Next Case**. Alternatively, you can go back to your work list of cases that require your attention by clicking **Case List**.

When you stop working, log out of Spectrum.

30. Click **Log Off** in the Spectrum toolbar and close the Internet browser.

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